Office Action Summary	Application No.	Applicant(s)	
	10/560,514	HILL ET AL.	
	Examiner	Art Unit	
	Stuart W. Snyder	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-80* is/are pending in the application.

4a) Of the above claim(s) *65-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-64 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 58-64 and newly added claim 80, in the reply filed on 11/27/2007 is acknowledged and examined herein; claims 65-79 are withdrawn from examination.

Drawings

2. The drawings are objected to because certain drawings do not have titles on the abscissa. For example, Figures 1, 7, 13, 19, 31, and 42 are titration curves of antibody responses to certain immunization protocols—apparently the abscissa merely indicates the different dilutions used in the ELISA experiments—but without a label on the abscissa it is difficult to compare the relative strength of the responses. Also, figure 49/56 illustrates the different IgG isotype responses to certain immunization protocols but the legend of the figure fails to differentiate between the two although the chart is self seems to have slightly different shading to indicate different IgG isotype. Similarly, from the legends of the two charts on page 54/56, it is difficult to differentiate between days 69 and 82 in Figure 65 or days 37 and 69 and days 82 and 105 in Figure 66; a similar problem exists with the legends of Figures 67 and 68 of page 55/56. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or

figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

3. The disclosure is objected to because of the following informalities: Although "Background of the Invention" and the "Detailed Description of the Invention" are in the specification, neither is labeled as such. Furthermore, the Examiner is unable to locate the sections "Brief Summary of the Invention" and "Brief Description of the Several Views of the Drawing" sections of the Specification. It would be very helpful to understand Applicants' view of the invention of the instant Application if the various sections were so labeled.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of

the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

Appropriate correction is required.

4. The abstract of the disclosure is objected to because the language is idiomatic. The abstract recites “relates to a vaccination". Although methods and compositions for various vaccination protocols are described in the specification, it is unclear from the abstract whether the aforementioned phrase refers to the procedure itself, the compositions used to practice the procedure or both. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 58-64 and 80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the subsections of claim 58 recites “a viral capsid substantially incapable of replication in a patient”. The recitation is ambiguous in at least two aspects: The phrase “substantially incapable of replication” is undefined leaving the subjective interpretation up to each reader and the word patient can refer to many categories of patients including veterinary patients or humans thus further obscuring the meaning of the first phrase because it is well known that some viruses, such as fowlpox viruses, can grow in some species, *e.g.*, chickens, but not others, *e.g.*, humans. Furthermore, each subsection of claim 58 recites the phrase “against which it is desired to obtain and immune response”. It is unclear from the claim language if

the desired immune response is against the antigen or the viral capsid or both. “A T-cell response” does not clarify the meaning of the phrase because T-cell responses can be very general such as cytokine release by some classes of stimulated T-cells or specific responses such as stimulation of reproduction of certain classes of antigen presenting cells, such as those identified in tetramer stimulation, *e.g.*, HLA B-27 subtype alleles in arthritic patients. Thus, the metes and bounds of the claims are unclear because of the ambiguities of the claim language.

6. Claim 64 and its dependent claim 80, each recite as examples of "capsids" MVA; claim 64 further recites "a poxvirus", "MVA or NYVAC", “an Orthopox virus” and “a fowlpox virus”. The Examiner has worked with Orthopox viruses previously and has a fair understanding of the terminology related to such viruses. In the event deeper or more specific understanding is required, the Examiner consults Field’s Virology as he has done in recently. The use of the word "capsid" generally refers to certain structures in certain enveloped viruses, such as HIV, and other non-enveloped viruses, such as poliovirus. However, the Examiner is not familiar with the term used in conjunction with Orthopox viruses. Referring to Chapter 74 of the 5th Edition of Field's Virology, the Examiner fails to see the term used except in reference to capsid proteins adventiously associated with or genetically engineered into the poxviruses. Thus, the only meaningful understanding of the use of the word “capsid” in claim 64 is in reference to an adenovirus; the term makes no sense in reference to poxviruses. For the

purposes of further examination, the Examiner with assign the word “capsid” in reference to *poxviridae* to mean either the MV or EV forms of the virion.

7. Claim 63 recites the limitation "vector" in the second line. There is insufficient antecedent basis for this limitation in the claim. Claim 63 depends on claim 58; claim 58 does not recite the word “vector”. Thus, there is no antecedent basis for the limitation “vector” in the claim.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 58-64 and 80 is rejected under 35 U.S.C. 102(b) as being anticipated by Feng, *et al.* The claims are drawn to a composition comprising a viral capsid (see definition above in reference to poxvirus "capsids") and an antigen, such composition being capable of inducing both a B-cell and T-cell immune response, such composition being formulated for co-administration or separate administration, said viral “capsid” of such composition consisting of a viral vector, such composition eliciting a protective T-cell response that may or may not be directed against said co-administered antigen, such composition inducing an antibody response that is greater than that induced by said antigen alone, and said composition comprising, *inter alia*, MVA and a *M. tuberculosis* antigen. Feng, *et al.* teaches induction of simultaneously a $CD8^+$ T-cell (see results and discussion) and an antibody response (see results, Table 1, page 572) to *M. tuberculosis*-encoded early secreted protein MPT64 under various immunization

protocols including various pulse-chase procedures (see especially Figure 4, page 572 and figure 5, page 573) and the B-cell response being greater when the vector (see Figure 2, page 571). Furthermore, Feng, et al. teaches that CD8+ T-cell activation is associated with protection and that the antigens used in their studies activated such T-cell association (see Introduction and throughout). Thus each and every limitation of claims 58-64 and 80 are taught by Feng, *et al.* which clearly anticipates the instantly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 58-64 and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huygen, *et al.* (1996) in view of Leong, *et al.* (1995)) and Sutter, *et al.* (1992). A summary of the limitations of the claims is found above (see section 8). Huygen *et al.* disclose a tuberculosis antigen, Ag85, in a DNA plasmid vector that induces THl-type T cell response and interferon gamma production (p.893, 3rd and 4th ¶) after being injected intraperitonially into mice three times (p.897, Methods, Vaccination). Huygen, *et al.* do not disclose boosting the CD4÷ T cell response with a poxvirus vector expressing the same antigen.

Leong, *et al.* disclose a method of generating enhanced immune responses against influenza by consecutive immunization with priming plasmid DNA

vectors, intramuscularly, and boosting recombinant fowl poxvirus vectors (FPV), intranasally (page 330). Leong, *et al.* further disclose that there are a number of advantages in using nonreplicating vectors for vaccine delivery. Immunization with naked DNA has been shown to be both safe and effective in generating prolonged immune responses. Similarly, recombinant FPV (rFPV) vectors have been tested in immunocompromised animals with no ill effects. However, both vectors tend to elicit relatively low titers of antibody, and multiple immunizations are required to generate a satisfactory immunity. By sequentially immunizing animals with DNA and rFPV expressing the same antigen, Leong, *et al.* were able to generate antibody responses equivalent to or greater than those detected in convalescent serum and far more than could be induced by either vector alone.

Neither Huygen, *et al.* nor Leong, *et al.* disclose boosting with a modified vaccinia virus Ankara strain (MVA) in the second composition. However, Sutter, *et al.* suggest using the non-replicating MVA to express recombinant genes (Abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the tuberculosis immunization method of Huygen, *et al.* by adding a boosting composition comprising a MVA or rFPV expressing the same antigen as suggested by Leong *et al.* and Sutter *et al.* The skilled artisan would have been motivated to do so to increase the level of antigen expression and thus enhance the CD4÷ T cell response against the tuberculosis antigen. There would have been a reasonable expectation of success because

Leong *et al.* specifically disclose that consecutive immunization with DNA and rFPV vectors showed better protection than immunization with either vector alone in a challenge study. Further, the reasonable expectation of success is established by the host-restriction of MVA and its safety in human, as taught by Sutter, *et al.*, and given that recombinant FPV (rFPV) vectors have been tested in immunocompromised animals with no ill effects, as taught by Leong, *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

10. No claims are allowed.

Correspondence

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stuart W Snyder
Examiner
Art Unit 1648

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